Diagnosis and management of primary aldosteronism in cats

Reusch, Claudia E

Primary Hyperaldosteronism

Prof. Dr. Claudia E. Reusch, DiplECVIM-CA

Aldosterone is secreted from the adrenal cortex under the control of the renin-angiotensin system and of potassium and to a lesser degree of ACTH. Its production is restricted to the zona glomerulosa because the enzyme aldosterone synthase is expressed zonal-specific. After secretion aldosterone binds to mineralocorticoid receptors which are present in the classical targets such as kidney, colon, sweat and salivary glands. Recently, it was shown that aldosterone is also synthesized in extra-adrenal tissues such as heart, brain and vasculature. In principle glucocorticoids and mineralocorticoids bind equally to the mineralocorticoid receptors, however, the enzyme 11β-hydroxysteroid dehydrogenase type 2 converts cortisol to the inactive cortisone, thereby preventing receptor-binding and enabling specificity of aldosterone action.

The consequences of increased aldosterone concentration are retention of sodium and water in the distal and collecting tubules of the kidneys. This results in increased intravascular volume and increased urinary potassium and hydrogen excretion. Excessive concentrations of circulating aldosterone also induce vasoconstriction and lead to an increase in peripheral vascular resistance. Additionally, aldosterone has pro-inflammatory and pro-fibrotic properties, leading to vascular, cardiac and renal lesions in the case of aldosterone excess.

The disease was first described in 1955 in a young woman by Jermone W. Conn, an American endocrinologist. The patient suffered from muscle spasm, weakness, hypertension and severe hypokalemia of several years duration. After extensive investigations over several months Conn came to the conclusion that the cause most likely was excessive secretion of aldosterone. In fact a tumor of the right adrenal gland was removed, which lead to complete recovery. Conn named the disease primary aldosteronisms, later it became also known as Conn's syndrome. After several years of research on this topic Conn postulated that primary aldosteronism is present in 10 – 20% of patients with hypertension: However, this was denied by most members of the medical profession who stated that the prevalence was less than 1%. Interestingly, a more systematic screening of hypertensive humans has recently shown that the prevalence is in fact much higher (5-10% of all patients with hypertension) and close to what has been assumed by Conn nearly half a century ago. In approximately 60% of human patients the disease is caused by bilateral idiopathic adrenal hyperplasia, while approximately 35% have aldosterone-producing adenomas. In a few patients unilateral adrenal hyperplasia, aldosterone-producing carcinomas or a specific form of familial hyperaldosteronism is present. Typical findings are systemic hypertension, hypokalemia and metabolic acidosis. The degree of hypertension is usually moderate to severe, and patients with aldosteronoma tend to have higher blood pressure than patients with idiopathic aldosteronism. Due to the fact that screening for the disease is becoming more systematic and the diagnosis is generally made earlier, the prevalence of hypokalemia is decreasing, and nowadays the majority of human patients are normokalemic at the time of diagnosis.

The first case of feline primary hyperaldosteronism was described in 1983. Since then, the disease has been diagnosed with increased frequency, and a little more than 30 cases have now been reported. Although no data are available concerning the true prevalence of the disease in the feline population, it is assumed that the disease is more common than initially thought. Feline primary hyperaldosteronism is a disease of middle aged to old cats (5 – 20 years), there appears to be no breed or sex predilection. Clinical sings include those caused by

a) hypokalemia (hypokalemic polymyopathy); such as cervical ventroflexion, hind limb weakness, ataxia or limb stiffness,

b) hypertension; such as intraocular hemorrhage, mydriasis and blindness due retinal detachment and hemorrhage.

Polyuria and polydipsia has also been seen in some cases, other non-specific signs such as anorexia, weight loss, lethargy, restlessness or panting may also be present. .
In the majority of cats with primary aldosteronism the disease is caused by unilateral carcinomas or adenomas, while bilateral tumors and bilateral nodular hyperplasia are less common. In cats with bilateral nodular hyperplasia the course of the disease is usually milder than in cats with other forms.
Almost all cats described to date have been hypokalemic at the time of diagnosis. However, as in human medicine, it may be possible that hyperaldosteronism is overlooked in cats with normal potassium levels. At our clinic we have recently seen cats which were normokalemic at presentation and hypokalemia was only seen after several days of hospitalization. A more systematic screening for primary hyperaldosteronism may improve diagnosis and thus increase the prevalence of the disease. Based on data available to date, the prevalence of hypertension in cats with primary aldosteronism appears to be high; the severity of hypertension ranged from mild to severe (185-270 mmHg).
Aldosterone excess also leads to renal acid excretion and metabolicalkalosis, which is usually mild. Additionally, hypophosphatemia may be present. Hyperaldosteronisms is often associated with slowly progressive renal disease, most likely due to hypertension and the profibrotic effects of aldosterone. Renal disease seems to be particular common in cats with bilateral nodular hyperplasia. Primary hyperaldosteronism should be diagnosed by means of hormone testing and diagnostic imaging. Hormone testing includes the demonstration of increased aldosterone and suppressed plasma renin activity, and increased aldosterone:renin ratio. Measurement of aldosterone alone is often insufficient: in cases of adrenocortical tumor aldosterone is usually highly elevated, however in cases with bilateral nodular hyperplasia aldosterone often is only slightly elevated or high-normal. It is important to remember that aldosterone may also be high in dehydrated animals without the disease (= secondary hyperaldosteronism). The measurement of the plasma renin activity is technically demanding and availability of the test is limited. Additionally, strict sampling and storage conditions have to be followed. Unfortunately, measurement of renin activity cannot be replaced by measurement of renin concentration (which is readily available) due to the lack of detection of feline renin by the antibody. Other tests, such as the fludrocortisone suppression test have been described, however its diagnostic utility needs further investigation.
Diagnostic imaging includes ultrasonography (or CT, MRI) of the abdomen with emphasis on the adrenal glands and possibly thoracic radiographs to search for metastasis. In cases in which the disease is due to an adrenal tumor usually the mass is easily found by ultrasonography. Very small masses, bilateral tumors and bilateral hyperplasia however pose a diagnostic challenge. Ultrasonography is also helpful to characterize extent of a tumor, possible invasion into the venal cava or other surrounding structures and metastasis.

Initial treatment should be directed towards alleviation of hypertension and hypokalemia by using an aldosterone antagonist (spironolactone 2.5 mg/kg q24h or 6.25 mg/cat q12h PO) and a calcium channel blocker (amlodipine besylate 0.625-1.25 mg/cat q24h PO), and substituting potassium as needed. Subsequent adrenalectomy is the treatment of choice for animals without tumor metastasis. Adrenalectomy is potentially curative, however due to the risk of perioperative complications (e.g. hemorrhage) the interventions should only be performed by an experienced surgeon. In cases in which adrenalectomy is not feasible (e.g. metastasized tumor, bilateral tumor or hyperplasia), medical treatment with spironolactone and amlodipine besylate should be continued. The two drugs combined seem to lead to resolution of hypertension in most cases

Galac S, Reusch CE, Kooistra HS and Rijnberk

Young WF

Refsal KR and Harvey AM